

WHAT IS CLAIMED IS:

- 7/26/94  
#10
1. An isolated nucleic acid encoding mammalian melanoma alpha kinase, wherein the nucleic acid is selected from the group consisting of :
    - a. the DNA sequence of SEQ ID NO: 28;
    - b. the DNA sequence of SEQ ID NO: 26;
    - c. DNA sequences that hybridize to the sequence of subparts (a) or (b) under standard hybridization conditions; and
    - d. DNA sequences capable of encoding the amino acid sequence encoded by the DNA sequences of subparts (a), (b) or (c).
  2. An isolated nucleic acid encoding human melanoma alpha kinase, wherein the nucleic acid comprises the DNA sequence of SEQ ID NO: 26.
  3. An isolated nucleic acid encoding mouse melanoma alpha kinase, wherein the nucleic acid comprises the DNA sequence of SEQ ID NO: 28.
  4. An isolated nucleic acid encoding mammalian heart alpha kinase, wherein the nucleic acid is selected from the group consisting of :
    - a. the DNA sequence of SEQ ID NO: 34;
    - b. the DNA sequence of SEQ ID NO: 36;
    - c. DNA sequences that hybridize to the sequence of subparts (a) or (b) under standard hybridization conditions; and
    - d. DNA sequences capable of encoding the amino acid sequence encoded by the DNA sequences of subparts (a), (b) or (c).
  5. An isolated nucleic acid encoding human heart alpha kinase, wherein the nucleic acid comprises the DNA sequence of SEQ ID NO: 34.
  6. An isolated nucleic acid encoding mouse heart alpha kinase, wherein the nucleic acid comprises the DNA sequence of SEQ ID NO: 36.

7. An isolated nucleic acid encoding mammalian kidney alpha kinase, wherein the nucleic acid is selected from the group consisting of :

- a. the DNA sequence of SEQ ID NO: 30;
- b. the DNA sequence of SEQ ID NO: 32;
- c. DNA sequences that hybridize to the sequence of subparts (a) or (b) under standard hybridization conditions; and
- d. DNA sequences capable of encoding the amino acid sequence encoded by the DNA sequences of subparts (a), (b) or (c).

8. An isolated nucleic acid encoding human kidney alpha kinase, wherein the nucleic acid comprises the DNA sequence of SEQ ID NO: 30.

9. An isolated nucleic acid encoding mouse kidney alpha kinase, wherein the nucleic acid comprises the DNA sequence of SEQ ID NO: 32.

10. In particular, the invention provides an isolated nucleic acid encoding mammalian skeletal muscle alpha kinase, wherein the nucleic acid is selected from the group consisting of :

- a. the DNA sequence of SEQ ID NO: 38;
- b. DNA sequences that hybridize to the sequence of subpart (a) under standard hybridization conditions; and
- c. DNA sequences capable of encoding the amino acid sequence encoded by the DNA sequences of (a) or (b).

11. An isolated nucleic acid encoding human skeletal muscle alpha kinase, wherein the nucleic acid comprises the DNA sequence of SEQ ID NO: 38.

12. An isolated nucleic acid encoding mammalian lymphocyte alpha kinase, wherein the nucleic acid is selected from the group consisting of :

- a. the DNA sequence of SEQ ID NO: 40;

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- b. DNA sequences that hybridize to the sequence of subpart (a) under standard hybridization conditions; and
  - c. DNA sequences capable of encoding the amino acid sequence encoded by the DNA sequences of (a) or (b).

13. An isolated nucleic acid encoding human lymphocyte alpha kinase, wherein the nucleic acid comprises the DNA sequence of SEQ ID NO: 40.

14. A recombinant DNA expression vector comprising the nucleic acid of any of Claims 1, 4, 7, 10 or 12, wherein the DNA encoding the alpha kinase is operatively associated with an expression control sequence.

15. A transformed host cell transfected with the DNA vector of claim 14.

16. A unicellular host transformed with a recombinant DNA molecule comprising a DNA sequence or degenerate variant thereof, which encodes an alpha kinase, or a fragment thereof, selected from the group consisting of:

- a. the DNA sequence of (SEQ ID NO: 26);
  - b. the DNA sequence of (SEQ ID NO: 28);
  - c. the DNA sequence of (SEQ ID NO: 30);
  - d. the DNA sequence of (SEQ ID NO: 32);
  - e. the DNA sequence of (SEQ ID NO: 34);
  - f. the DNA sequence of (SEQ ID NO: 36);
  - g. the DNA sequence of (SEQ ID NO: 38);
  - h. the DNA sequence of (SEQ ID NO: 40);
  - i. DNA sequences that hybridize to any of the foregoing DNA sequences under standard hybridization conditions; and
  - j. DNA sequences that code on expression for an amino acid sequence encoded by any of the foregoing DNA sequences;
- wherein said DNA sequence is operatively linked to an expression control sequence.

17. The unicellular host of Claim 16 wherein the unicellular host is selected from the group consisting of *E. coli*, *Pseudomonas*, *Bacillus*, *Streptomyces*, yeasts, CHO, R1.1, B-W, L-M, COS 1, COS 7, BSC1, BSC40, and BMT10 cells, plant cells, insect cells, mouse cells and human cells in tissue culture.

18. An isolated protein characterized by the presence of at least two domains, one of the domains being an alpha-kinase catalytic domain and the other domain being an ion channel domain.

19. An isolated melanoma alpha kinase protein characterized by having an alpha-kinase catalytic domain and an ion channel domain.

20. The melanoma alpha kinase protein of Claim 19 which comprises the amino acid sequence set out in SEQ ID NO: 27 or 29, and variants thereof wherein one or more amino acids is substituted with a conserved amino acid.

21. An isolated kidney alpha kinase protein characterized by having an alpha-kinase catalytic domain and an ion channel domain.

22. The kidney alpha kinase protein of Claim 21 which comprises the amino acid sequence set out in SEQ ID NO: 31 or 33, and variants thereof wherein one or more amino acids is substituted with a conserved amino acid.

23. An isolated heart alpha kinase protein.

24. The heart alpha kinase protein of Claim 23 which comprises the amino acid sequence set out in SEQ ID NO: 35 or 37, and variants thereof wherein one or more amino acids is substituted with a conserved amino acid.

25. An isolated skeletal muscle alpha kinase protein.

26. The skeletal muscle alpha kinase protein of Claim 25 which comprises the amino acid sequence set out in SEQ ID NO: 39, and variants thereof wherein one or more amino acids is substituted with a conserved amino acid.

27. An isolated lymphocyte alpha kinase protein.

28. The lymphocyte alpha kinase protein of Claim 27 which comprises the amino acid sequence set out in SEQ ID NO: 41, and variants thereof wherein one or more amino acids is substituted with a conserved amino acid.

29. A pharmaceutical composition comprising one or more alpha kinase protein selected from the group of melanoma alpha kinase, kidney alpha kinase, heart alpha kinase, skeletal muscle alpha kinase and lymphocyte alpha kinase, and a pharmaceutically acceptable carrier.

30. A purified antibody to an alpha kinase protein selected from the group of melanoma alpha kinase, kidney alpha kinase, heart alpha kinase, skeletal muscle alpha kinase and lymphocyte alpha kinase.

31. A monoclonal antibody to an alpha kinase protein selected from the group of melanoma alpha kinase, kidney alpha kinase, heart alpha kinase, skeletal muscle alpha kinase and lymphocyte alpha kinase

32. An immortal cell line that produces a monoclonal antibody according to Claim 31.

33. The antibody of any of Claims 30 or 31 labeled with a detectable label.

34. The antibody of Claim 33 wherein the label is selected from the group consisting of an enzyme, a chemical which fluoresces, and a radioactive elements.

35. The antibody of any of Claims 30 or 31 which recognizes the phosphorylated form of the alpha kinase or a phosphorylated fragment thereof.

36. A method for treating an animal in need of increased activity of melanoma alpha kinase which comprises administration of melanoma alpha kinase to the animal.

37. A method for treating an animal in need of increased activity of melanoma alpha kinase which comprises administration of an antibody against melanoma alpha kinase to the animal.

38. A method for treating an animal in need of increased activity of kidney alpha kinase which comprises administration of kidney alpha kinase to the animal.

39. A method for treating an animal in need of increased activity of kidney alpha kinase which comprises administration of an antibody against kidney alpha kinase to the animal.

40. A method for treating an animal in need of increased activity of heart alpha kinase which comprises administration of heart alpha kinase to the animal.

41. A method for treating an animal in need of increased activity of heart alpha kinase which comprises administration of an antibody against heart alpha kinase to the animal.

42. A method for treating an animal in need of increased activity of skeletal muscle alpha kinase which comprises administration of skeletal muscle alpha kinase to the animal.

43. A method for treating an animal in need of increased activity of skeletal muscle alpha kinase which comprises administration of an antibody against skeletal muscle alpha kinase to the animal.

44. A method for treating an animal in need of increased activity of lymphocyte alpha kinase which comprises administration of lymphocyte alpha kinase to the animal.

45. A method for treating an animal in need of increased activity of lymphocyte alpha kinase which comprises administration of an antibody against lymphocyte alpha kinase to the animal.

46. A method for detecting the presence or activity of an alpha kinase protein selected from the group of melanoma alpha kinase, kidney alpha kinase, heart alpha kinase, skeletal muscle alpha kinase and lymphocyte alpha kinase, wherein said alpha kinase is measured by:

A. contacting a biological sample from a mammal in which the presence or activity of said alpha kinase is suspected with a binding partner of said alpha kinase under conditions that allow binding of said alpha kinase to said binding partner to occur; and

B. detecting whether binding has occurred between said alpha kinase from said sample and the binding partner;

wherein the detection of binding indicates that presence or activity of said alpha kinase in said sample.

47. A method for detecting the presence of an alpha kinase protein selected from the group of melanoma alpha kinase, kidney alpha kinase, heart alpha kinase, skeletal muscle alpha kinase and lymphocyte alpha kinase, wherein the alpha kinase is measured by:

a. contacting a sample in which the presence or activity of an alpha kinase protein selected from the group of melanoma alpha kinase, kidney alpha kinase, heart alpha kinase, skeletal muscle alpha kinase and lymphocyte alpha kinase is suspected with an antibody to the said alpha kinase protein under conditions that allow binding of the alpha kinase protein to the binding partner to occur; and

- b. detecting whether binding has occurred between the alpha kinase protein from the sample and the antibody;

wherein the detection of binding indicates the presence or activity of the alpha kinase protein in the sample.

48. A method of testing the ability of a drug or other entity to modulate the kinase activity of an alpha kinase protein selected from the group of melanoma alpha kinase, kidney alpha kinase, heart alpha kinase, skeletal muscle alpha kinase and lymphocyte alpha kinase which comprises:

- A. culturing a colony of test cells containing the alpha kinase protein;
- B. adding the drug or other entity under test; and
- C. measuring the kinase activity of said alpha kinase protein in the test

cells, wherein when the amount of kinase activity in the presence of the modulator is greater than in its absence, the modulator is identified as an agonist or activator of the alpha kinase protein, whereas when the amount of kinase activity in the presence of the modulator is less than in its absence, the modulator is identified as an antagonist or inhibitor of the alpha kinase protein.